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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/090,849 | 03/04/2002 | Peter David Rathjen | 18377-0010 | 5909 |
| 46272 | 7590 | 04/01/2005 | EXAMINER | |
| Sutherland, Asbill & Brennan/Atta: Bill Warren 999 Peachtree Street, NE Atlanta, GA 30309-3996 | | | GAMETT, DANIEL C | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1647 | |

DATE MAILED: 04/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/090,849

Applicant(s)

RATHJEN ET AL.

Examiner

Daniel C. Gamett

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 February 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 18-25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 March 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>01/14/2003</u> . | 6) <input type="checkbox"/> Other: _____ |

JL

DETAILED ACTION

1. Applicant's election without traverse of Claims 1-17 in the reply filed on 02/22/2005 is acknowledged. Claims 18-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 02/22/2005.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1, 2, 4, 5, and 6 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/181359. Although the conflicting claims are not identical, they are not patentably distinct from each other because each step of instant claim 1 and claims dependent therefrom is either a genus anticipated by a species in Claim 1 of 10/181359 or is fully identical in scope to Claim 1 of 10/181359.

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Claim 1 in the instant case recites (outline headings added):

1. A method for the preparation of cells of ectodermal or endodermal lineages, of high purity which method includes
 - i. providing
 - (1) a source of pluripotent cells,
 - (2) a source of a mesodermal suppression composition including cellular fibronectin (cFN); and
 - (3) a suitable culture medium, and
 - ii. culturing the pluripotent cells in the culture medium in the presence of the mesodermal suppression composition for a time sufficient to permit differentiation to ectoderm cells.

Claim 1 of 10/181359 recites (outline headings added):

1. A method of producing neuroectoderm cells, which method includes
 - i. providing
 - (1) a source of early primitive ectoderm-like (EPL) cells;
 - (2) a conditioned medium as hereinbefore described; or an extract therefrom exhibiting neural inducing properties; and
 - ii. contacting the EPL cells with the conditioned medium or extract, for a time sufficient to generate controlled differentiation to neuroectoderm cells.

The claims are related as follows:

- Preamble and step ii: “neuroectoderm cells” is a species of “cells of ectodermal or endodermal lineages”.
 - Instant claim 2 limits the ectodermal cells of the preamble to “neuroectoderm cells or surface ectoderm” and thus recites the same species as in claim 1 of 10/181359.
- Method step i(1): “early primitive ectoderm-like (EPL) cells” are a species of “pluripotent cells”.
 - Instant claims 4 and 5 each recite EPL cells as their source of pluripotent cells and thus they recite the same species as in claim 1 of 10/181359.
- Method step i(2): The instant specification states on p. 6, lines 9-11, that, “The source of cFN may be cFN itself, or a conditioned medium as described in International patent application PCT/AU99/00265 above, or an extract thereof containing cFN.” 10/181359 states on p. 10, lines 7-9, “The conditioned medium utilised in the method according to the present invention is described in International patent application W099/53021, the entire disclosure of which is incorporated herein by reference.” PCT/AU99/00265 and

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W099/53021 are one in the same (Bettess *et al*, item AE in the IDS filed January 14, 2003), and therefore the “a source of a mesodermal suppression composition including cellular fibronectin” and “a conditioned medium as hereinbefore described” are equivalent. That is, the media of method step (2) are identical for both claims.

- The limitations of instant claim 6, that the mesodermal suppression composition source is selected from the group consisting of cellular fibronectin, MEDII, a conditioned medium, or an extract thereof containing cellular fibronectin, fall within the scope of 10/181359, claim 1.
- Method step i(3) of the instant claim, “a suitable culture medium” is not specifically recited in 10/181359, claim 1, but this is implicit in the latter method. Obviously, the cells must be in suitable culture medium for the method to work.

Therefore, instant Claims 1, 2, 4, 5, 6, and claim 1 from 10/181359 all recite methods in which the same type of cell is subjected to same steps of incubation leading to the same outcome. The differences between the claims are that the material described in step i(2) is described as being “a mesodermal suppression composition including cellular fibronectin” in the instant case and as “a conditioned medium as hereinbefore described; or an extract therefrom exhibiting neural inducing properties” in 10/181359. Additionally the instant claims 1, 4, 5, and 6 hold open the possibility of producing endodermal cells, which is not recited in 10/181359, claim 1. There is no indication in either specification or in the claims that the compositions described in step i(2) are materially different; they both are the same conditioned medium disclosed by Bettess in W099/53021. Therefore it appears that said conditioned medium inherently comprises cellular fibronectin and is inherently capable of mesodermal suppression, neural induction, and endodermal induction.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

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4. Claims 9-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-15 of copending Application No. 10/181359. Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the limitations added in the instant claims is either a genus anticipated by a species in Claims 12-15 of 10/181359 or is fully identical in scope to Claims 12-15 of 10/181359, and said limitations were added to base claims that are deemed obvious over one another as described above.

Claim 9 in the instant case recites (outline headings added):

9. A method for the preparation of cells of ectodermal or endodermal lineages, of high purity which method includes
 - i. providing
 - (1) a source of pluripotent cells,
 - (2) a source of a mesodermal suppression composition including cellular fibronectin (cFN);
 - (3) a suitable culture medium, and
 - (4) a growth factor
 - ii. culturing the pluripotent cells in the culture medium in the presence of the cFN source and growth factor.

Thus, instant claim 9 is identical to instant claim 1 except for the additional provision of a growth factor present in the culture medium. Correspondingly, claim 12 of 10/181359 is related to claim 1 of 10/181359 through dependencies from claims 4 and 2, resulting in the following:

12. A method of producing neuroectoderm cells, which method includes
 - i. providing
 - (1) a source of early primitive ectoderm-like (EPL) cells;
 - (2) a conditioned medium as hereinbefore described; or an extract therefrom exhibiting neural inducing properties; and
 - ii. contacting the EPL cells with the conditioned medium or extract, for a time sufficient to generate controlled differentiation to early neuroectoderm cells.
 - iii. Further culturing the early neuroectoderm cells in the presence of a growth factor of the FGF family while late neuroectoderm cells are formed.

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Thus, claim 12 of 10/181359 differs from claim 1 of 10/181359 by the recitation of early neuroectoderm and then late ectoderm cells as the product of the method, and by the provision of a growth factor of the FGF family in the medium.

The instant claim 9 and claims dependent therefrom are related to claim 12 of 10/181359 and claims dependent therefrom as follows:

- The preambles, and steps i(1), i(2), and i(3) are identical to the respective claims 1 and so are related to one another as described above for instant claim 1 and claim 1 of 10/181359.
- The products recited in parts ii and iii in claim 12 of 10/181359, early and late ectodermal cells, respectively, are each species of the genus “cells of ectodermal or endodermal lineages” recited in instant claims 9 and 1, and the genus “neuroectoderm cell” recited in instant claim 10.
- “a growth factor of the FGF family” (10/181359 claim 12, iii) is a species of the genus “growth factor” (instant claim 9, i(4) and ii).
- Claim 12 of 10/181359 recites a growth factor of the FGF family and so is identical in scope to instant claim 11, with respect to the growth factor component.
- The individual FGF family members recited in 10/181359 claims 13 and 14 are species within the genus of “growth factor” (instant claim 9) and “growth factor of the FGF family” (instant claim 11). Conversely, the individual FGF family members recited in instant claims 12-14 are species within the genus of “growth factor of the FGF family” (10/181359 claim 12). Instant claims 12 and 14 are identical in scope to 10/181359 claims 13 and 14, respectively, with respect to the growth factor component.
- Claims 15 from both applications recite the FGF growth factor in a concentration range of approximately 1 to 100 ng/ml and so they are identical in scope with respect to the growth factor component.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

35 U.S.C. § 112, Second Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is drawn to a method for the preparation of cells of ectodermal or endodermal lineages, of high purity. The final step of the method, recites culturing cells for a “time sufficient to permit differentiation to ectoderm cells”. Thus, the method does not appear to achieve the goal of preparing endodermal cells stated in the preamble.
7. Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 9 is drawn to a method for the preparation of cells of ectodermal or endodermal lineages, of high purity. Said method does not include a final step in which the goal of preparing ectodermal or endodermal cells is achieved.

35 U.S.C. § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Bettess *et al.*, International patent application W099/53021, published 21 October, 1999 (item AE in the IDS filed January 14, 2003; hereafter 'Bettess'). All claims depend from claims 1 or 9, which specify the starting cell, conditioned media, growth factor, and differentiated cell product limitations. Said limitations are taught in Bettess as follows: Bettess teaches on p. 18: "*For example, maintaining contact of EPL cells [a source of pluripotential cells, as in all instant claims; specifically recited in claims 4 and 5] with the conditioned medium, biologically active factor, or components thereof [as in all instant claims; see section 3, above, for discussion of the equivalency of the conditioned medium disclosed by Bettess and the conditioned medium of the instant specification.], preferably in cell aggregates grown in suspension, preferably in the presence of a growth factor from the, FGF family [as in claims 9-17] such as FGF4 [specifically recited in claims 12 and 13], may be used to produce an at least partially differentiated cell type equivalent to embryonic neuroectoderm, which can differentiate further to a range of neural cell types [instant claims 1, 2, 4-17].*" Bettess' Figures 24 and 25 show endoderm formation from EPL cells [claim 3]. Figures 19-21 indicate that cellular fibronectin is an active component of conditioned medium [all instant claims, specifically recited in claim 6]. Differentiation to neuroectoderm was detected at 3 days of culture (figure 21), which is within the 2-6 day limitation of claim 7. Example 1, p.39, indicates that high glucose DMEM [claim 8] was the base medium for the experiments disclosed in Bettess. Figures 29 and 32 show differentiation to neuroectoderm in presence of bFGF and FGF4, respectively [claims 9-17]; the respective FGF concentrations are 10 ng/ml and 20 ng/ml, thus anticipating the "approximately 10 ng/ml" limitation for bFGF in claim

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17, and the 1-100 ng/ml and 5-50 ng/ml ranges recited in claims 15 and 16. Therefore, all of the starting cell, growth factor, concentration, time, and differentiated cell product limitations of claims 1-17 were previously disclosed in Bettess.

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Lake et al., (2000) J. Cell Science 113, 555-566 and Rathjen et al., (1999) J. Cell Science 112, 601-612, items AF and AG, respectively, on the IDS filed January 14, 2003 are equivalent to Bettess *et al.*, International patent application W099/53021 in anticipating claims 1-17.

Conclusion

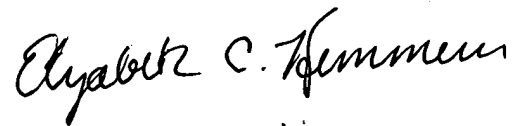
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D., whose telephone number is 571 272 1853. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DCG
Art Unit 1647
22 March 2005



**ELIZABETH KEMMERER
PRIMARY EXAMINER**